ORIGINAL ARTICLE

Herd Reproduction Ratio and Time–Space Analysis of a Foot-and-mouth Disease Epidemic in Peru in 2004

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Summary

The herd reproductive ratio (R_h) and spatio-temporal clustering were estimated in the 2004 foot-and-mouth disease (FMD) epidemic in Peru. The epidemic lasted 39 days and involved 26 herds. Movement of cattle was restricted, all susceptible species within a 25-km buffer zone were revaccinated, and infected animals with clinical signs of FMD were killed or destroyed to control and eradicate the disease. The R_h declined from 5.3 on the second day of the epidemic to 1.31 on the 25th day. Spatio-temporal clustering of cases was detected at a critical distance of 0.5 km and critical times of 7 and 14 days. Cases were clustered in space ($P = 0.006$) but not in time ($P = 0.498$). The space–time scan method detected a spatio-temporal cluster that included consecutive case numbers 13, 14 and 15, located at the temporal midpoint of the epidemic. The values estimated for R_h and the cluster analyses provide quantitative estimates of the self-limiting nature of FMD spread in a susceptible but vaccinated population.

Introduction

Foot-and-mouth disease (FMD) is a highly infectious vesicular disease of cloven hoofed animals, including cattle, sheep, swine, goats and camelids (Sharma et al., 1981; Wernery and Kaaden, 2004). It is caused by one of seven immunologically distinct serotypes of an aphtovirus (FMDv) of the family Picornaviridae, O, A, C, SAT (South African Territories) 1, 2 and 3, and Asia 1, of which 61 virus subtypes have been characterized (Saiz et al., 2002). Clinical disease is typically characterized by vesicles and erosions on the tongue, nose, muzzle, coronary bands and teats (Moonen et al., 2004). Foot-and-mouth disease is considered one of the most important livestock diseases in the world because of its substantial economic and trade impact, which includes lost revenues from reduced herd productivity, increased costs of animal health programmes and reduced exports to countries prohibiting trade of animals and animal products with countries with FMD (Zottele and Astudillo, 1991).

Foot-and-mouth disease was first reported in South America at the end of the 19th century, in Argentina, Uruguay and Brazil, and then spreading to other South American countries (Rodriguez-Torres, 2000). It was first described in Peru in 1910. Since the 1990s, the number of FMD epidemics in Peru has decreased (SENASA, 2004a). The FMD control programme in Peru has required biannual FMD vaccination in geographical regions where the risk of new cases of FMD is considered to be elevated. No cases of FMD had been reported in Peru between October 2000 and June 2004. However, on June 11th 2004, an epidemic caused by serotype O FMD virus was reported in the department of Lima. No region in Peru was FMD-free recognized by the Office International des Epizooties (OIE) at the time of the epidemic. The area where the FMD-affected herds were detected was not in the FMD-free zone where vaccination is not practiced

established in Peru in December 2004 and recognized by the OIE in May 2005.

Epidemics where details of incident cases have been accurately recorded provide opportunities to gain insight into the epidemiology of infectious diseases. Such insight can help improve specific actions taken to prevent, control and eradicate subsequent cases and epidemics. For example, data can be obtained to calculate the herd reproductive ratio (R_h), which is an estimate of the number of susceptible herds infected by one infected herd (Anderson and May, 1991). Changes in the ratio during the course of an epidemic reflect changing numbers of susceptible animals and/or contacts between susceptible and infectious animals as a consequence of implementation of control measures like vaccination or movement restrictions. Field estimates of R_h can be useful in modelling exercises to simulate transmission and spread of disease in areas not yet affected by FMD, which can provide an understanding of the magnitude of a future epidemic. Projections of where and when the disease is most likely to spread can be used in planning surveillance and control strategies, and in estimating potential costs and needed resources for disease surveillance and control.

The objectives of this paper were to describe the course of the FMD epidemic in Peru in 2004 and to estimate the R_h and the nature and extent of any spatio-temporal clustering of reported cases.

Materials and Methods

Epidemic information

The previous epidemic of FMD in Peru was in 2000, which involved serotype A of the FMDv. Serotype O of FMDv was last isolated in Peru in 1997. The disease or disease agent was not detected in national surveys between 2000 and 2004 (SENASA, 2004a).

Peru is administratively divided into 24 primary administrative areas, which are referred to as departments. Departments are subsequently divided into secondary administrative areas referred to as provinces. Officially supervised FMD vaccination of cattle was mandatory in some provinces within the departments of Tumbes, Cajamarca and Lambayeque, located in the northwest region and in some provinces within the departments of Ancash and Lima in the central coast (SENASA, 2004a). Those cattle were vaccinated twice a year, between April and May, and between September and October. Cattle moved from a region where vaccination was not mandatory to a region where it was mandatory were required to be vaccinated for FMD within 2 days after they entered the region where vaccination was mandatory and a booster was required 30 days after the first vaccination. The vaccine contained strains of the FMD virus serotypes A_{24} Cruzeiro and O_1 Campos and an oil adjuvant. All cattle imported to Peru from countries where FMD was endemic were vaccinated at control posts close to the borders and a certificate of vaccination was issued for each animal to be transported within Peru. Susceptible animals introduced into the area under vaccination but that were intended to be killed within 15 days from the introduction into the area, were not vaccinated (Gobierno de Peru, 2004).

On June 11th 2004, FMD-like signs were reported in a herd located in the district of Lurin, department of Lima, 40 km south of Lima. The herd had received replacement animals a week before clinical signs were observed. Samples of serum and oral epithelium were collected from animals showing clinical signs, and the specimens were tested at the Laboratorio de Sanidad Animal in Lima for evidence of FMD virus by methods of virus isolation (Clarke and Spier, 1980), FMDv antigen detection, using virus infection-associated antigen assay (McVicar and Sutmoller, 1970), antibody detection, using an ELISA (Ferris and Dawson, 1988), and an enzyme-linked immunoelectrotransfer blot (EITB) for antibodies against nonstructural FMDv proteins (Bergmann et al., 2000). During the following 5 weeks, animals in another 25 herds were confirmed by virus isolation to be infected by an FMDv serotype O (Table 1). All case herds were located within a 4-km radius in the districts of Lurin and Pachacamac (Fig. 1). The herds in which the cases were reported were designated as infected zones and a buffer zone of 25 km radius was established centered on the index case (Fig. 1). Control measures were implemented the first day FMD was diagnosed in a herd. Measures within the buffer zone included restricted movement of people, animals and motorized vehicles. All susceptible species, including cattle, swine, sheep, goats and camelids within the buffer zone were vaccinated using the same vaccine and dosage used previously for routine vaccination. The infected cattle in the herds diagnosed during the first 2 days of the epidemic were killed and the carcasses were incinerated (SENASA, 2004b). Thereafter, cattle that tested positive for FMD were killed and the carcasses were deboned and sold for commercial use (Table 1). The last case of FMD was diagnosed on July 19, 2004, and the emergency control measures were suspended on September 3, 2004. Origin of the replacement animals in the index herd could not be verified.

The nucleotide sequences of the VP1 gene of four viruses isolated in the FMD epidemic of 2004 were characterized by the laboratory of the Unidad de Salud Publica Veterinaria at the Centro Pan-Americano de Fiebre Aftosa (PANAFTOSA). Results of the neighbour-joining method, comparing 639 nucleotide sequences of the VP1 gene indicated that viruses isolated in this epidemic were

Table 1. Time distribution, number of confirmed clinical cases, and time-to- report a case in the 2004 foot-and-mouth disease epidemic in Peru

Case number	Day of epidemic	Number of cattle in herd	Number tested positive[a]	Time-to-report (days)
1	1	812	1[b]	7
2	2	171	4[b]	14
3	2	159	3[b]	11
4	11	213	2[c]	16
5	11	88	10[c]	2
6	11	43	2[c]	16
7	11	117	1[c]	2
8	13	380	5[c]	1
9	16	46	11[c]	16
10	18	60	18[c]	5
11	18	63	1[c]	1
12	18	93	1[c]	4
13	19	18	4[c]	3
14	19	105	7[c]	4
15	19	29	17[c]	14
16	25	21	3[c]	4
17	25	186	9[c]	2
18	26	15	1[c]	1
19	27	11	2[c]	2
20	27	3	3[c]	0
21	28	26	2[c]	2
22	29	4	1[c]	0
23	32	76	9[c]	2
24	35	17	5[c]	0
25	39	186	9[c]	16
26[d]	39	47	1[c]	4

[a]Tested positive by serology and/or by virus isolation.
[b]Those tested positive were euthanized and destroyed/incinerated.
[c]Those tested positive were slaughtered and carcasses were deboned.
[d]Last case diagnosed.

identical to each other. Compared with the VP1 gene of an isolate of FMDv obtained during the 2002 FMD epidemic in Ecuador, 96% of the nucleotides were identical in the four 2004 Peruvian isolates (PANAFTOSA 2004).

Data source and general approach

Data and information regarding control measures taken during the FMD epidemic in Peru in 2004 were obtained from reports issued by SENASA in Peru. Records obtained included the date the owner identified lesions, the date an official veterinarian investigated the case, the location of the affected herd and the total number of susceptible and infected animals in the herd. Telephone and e-mail communications with government officials from Peru were also used to add information not included in the reports and to clarify and expand the information collected in the reports. A case or FMD-affected herd was

defined here as a herd in which at least one FMD-infected animal was identified. The location of the cases (Fig. 1) indicates the geographical location of FMD-infected animals, as recorded by SENASA at the time of intervention of the affected herds.

Herd reproductive ratio

The herd reproductive ratio (R_h) estimates the number of new herds that will become infected as a result of direct or indirect contact with a herd that is infected. It is calculated as $R_h = 1 + (D/t_d) \ln 2$ (Anderson and May, 1991), where D is the duration of infectiousness (days) of each case, here defined as a herd in which FMD had been diagnosed with duration D being the aggregate time of all infected animals in the herd shedding the virus and t_d is the time interval (days) within which the number of detected cases doubled. Duration of infectiousness was considered to be the sum of the days for the subclinical infectious period, for the time from observation of signs to reporting by the owner, referred to here as time-to-report and for the time from reporting by the owner to diagnosis by the laboratory (time-from-report-to-diagnosis). The subclinical infectious period was defined as the number of days between the beginning of virus shedding and appearance of clinical signs, which had been estimated to be between 2 and 5 days (Burrows, 1968). Time-to-report was obtained from official records of the epidemic. Time-from-report-to-diagnosis was assumed to take a minimum value of 1 day, a most likely value of 2 days and a maximum value of 4 days (Bates et al., 2003). Samples were collected and submitted to the reference laboratory by official veterinarians. Therefore, veterinary services were already alerted of the potential occurrence of an FMD case at the time of FMD diagnosis. For that reason and because of the low number of FMD-affected herds, it has been estimated that intervention of FMD-affected herds occurred within the day in which an FMD-positive diagnostic was made. Thus, time-from-diagnostic-to-intervention was assumed to be nil. For purposes of analysis, it was assumed that the sum of the subclinical infectious period and time-from-report-to-diagnosis followed a Pert distribution of (3, 5, 9) days. The values of the Pert distribution for the sum of the subclinical infectious period and time-from-report-to-diagnosis were added to the time-to-report value for each FMD-affected herd to obtain a Pert distribution for duration of infectiousness for each individual case. The assumption of a Pert distribution for duration of infectiousness was necessary because no realistic information was available to us on the value that subclinical infectious period and time-from-report-to-diagnosis took on each individual
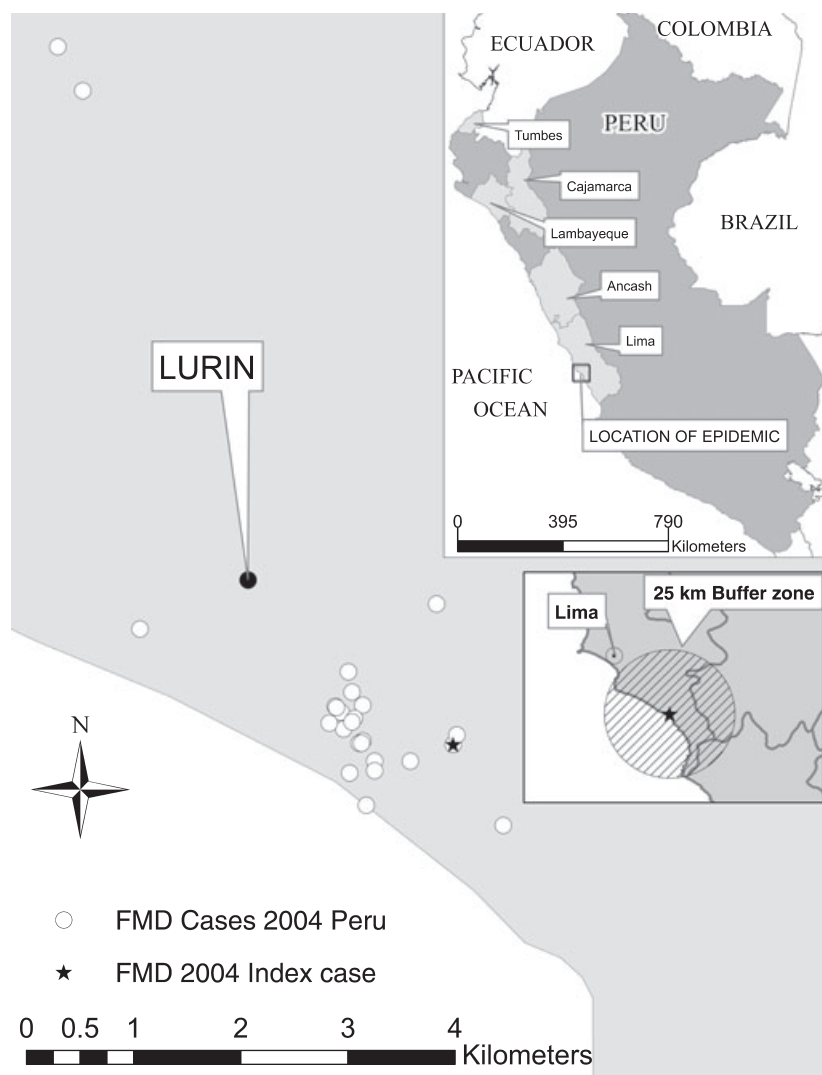
Fig. 1. Geographical distribution of cases and location of the 25 km buffer zone during the 2004 foot-and-mouth disease (FMD) epidemic in Peru. Boundaries of departments with FMD-affected herds are indicated.

case. Assumption of a distribution to describe the uncertainty on the value that certain parameters have in the field is a standard technique in stochastic modelling. The Pert distribution assumed here provides an estimate of the uncertainty that the authors have on the real value of the sum of the subclinical infectious period and time-from-report-to-diagnosis for each individual case. The value of R_h was computed on 999 simulations for each day d by which the number of case doubled the number of affected herds previously detected, i.e. on each day d in which it was possible to estimate the value of t_d. Therefore, the value of R_h was computed for several periods of the epidemic, each of these periods determined by the interval of time between 2 days in which the number of affected herds was doubled. For each of the 999 simulations, a random value was withdrawn from the Pert distribution assumed for duration of infec-

tiousness. This procedure resulted in the computation of a 95% confidence interval for the value of R_h, which reflects the most likely, maximum and minimum value estimated for R_h in the field, given the values and assumptions used in the calculations. R_h cannot be estimated for the period of time elapsed between the last day by which the number of cases doubled the number of affected herds previously reported and the end of the epidemic, because of the impossibility to calculate the value of t_d. Thus, a value of $R_h < 1$ was assumed for the last period of the epidemic, when the value of t_d could not be computed.

A value of $R_h > 1$ indicates that the number of new cases was increasing; $R_h = 1$ means that the number of new cases remains constant; and $R_h < 1$ means that the number of new cases is decreasing (Anderson and May, 1991).

Space–time analyses

The Knox's test (Knox, 1964) and the space–time permutation scan statistic (Kulldorff et al., 2005) were used to assess spatio-temporal clustering of cases during the epidemic. Calculations for a Knox test were performed using SSTAT Spatial Statistics Program V4.7, and calculations for the time–space scan method were performed using SATSCAN v5.1™ (Kulldorff and Information Management Services, Inc, 2003). The Knox test evaluated the likelihood of clusters of cases in space and time without specifying which specific cases contributed to the clusters; whereas, the space–time scan method indicates which cases constituted which specific clusters. Both tests statistics were computed considering the estimated infection date and geographical location of the affected herds provided by SENASA.

Knox's test

Each case was paired with each of the other cases to form $[n(n-1)]/2$ pairs of cases, where n was the total number of cases observed during the epidemic ($n = 26$; observed pairs of cases = 325). The time and distance relationship between the pairs of cases were summarized in a 3×5 contingency table where the column values indicated time, limited by less than the critical time or more than the critical time, and the row values indicated distance, as limited by less than the critical distance or more than the critical distance. Separation of a pair of cases in time by less than the value defined for critical time was interpreted to indicate time clustering of the pair of cases. Separation of a pair of cases in distance by less than the value defined for critical distance was interpreted to indicate spatial clustering of the pair of cases (Ward and Carpenter, 2000).

Three critical times (X_t) of 7, 14 and 21 days were used to estimate the expected number of pairs of cases for specified critical distances. For each value of X_t, five critical distances (X_d) were applied, starting with the maximum distance between cases and decreasing by half for each subsequent distance value to give distances of 8, 4, 2, 1 and 0.5 km. The product of the marginal sum for the row and the marginal sum for the column was divided by the total number of observed pairs of cases to provide an expected number of pairs of cases with evidence of spatio-temporal clustering. The difference between the observed and the expected numbers of pairs of cases ($Y_{t,d}$) was calculated for each combination of X_t and X_d. Univariate regression analyses were used to estimate the association between X_t and X_d (independent variables) and $Y_{t,d}$ (dependant variable). Confidence intervals generated for the regression coefficients that included zero were interpreted to indicate that the variable (X_t, X_d) was not linearly associated with increase in the intensity of clustering, defined here as difference between the observed and the expected numbers of pairs of cases (Student's t-test, $P < 0.05$).

The null hypothesis that the time interval between a pair of cases was independent of the geographical distance between a pair of cases or, stated in other words, that there was no clustering of cases in space and time, was tested by comparing the observed time intervals between cases with expected time intervals, which were estimated using 999 Monte Carlo simulations of randomized time intervals between cases while retaining the observed space distance between cases. A P-value was estimated as the proportion of the 999 simulations in which the simulated number of pairs of cases separated by less than X_t and X_d was less than the observed number of pairs of cases separated by less than X_t and X_d. The null hypothesis was rejected if the P-value was less than 0.05.

Diggle et al., 1995, extended Ripley's K-function for assessment of spatial clustering into a test for time–space clustering similar to the application of the Knox test used here. The main advantages of using the space–time K-function, compared with the Knox test, is the ability to adjust for a potential edge effect and that temporal and spatial separation between pairs of outbreaks, rather than spatial and temporal thresholds, are used to compute the statistic. In the absence of edge effect, results of the application of the Knox test described here are expected to be similar to those obtained by the application of a space–time K-function. No edge effect was present in our database and use of temporal and spatial thresholds was functional to the application of a regression analysis to quantify the influence of time and space in clustering. For those reasons, the Knox test-based approach described here was preferred.

Space–time permutation scan statistic

Another method for assessing a space–time relationship is the space–time scan statistic, which centers a hypothetical time–space cylinder at the geospatial coordinates of each location where information is available. The base and the height of the cylinder represent the respective geographical and the temporal dimensions of the cases, as estimated by the analytic method. Values for the maximum radius of the cylinder base and the maximum height of the cylinder varied and had to be set *a priori* based on knowledge about the epidemiology of the disease or on the purpose of the study. The space–time scan statistic compares the risk, defined as the ratio between the number of cases and the number at risk, of finding a case within the area inside the cylinder with the risk of finding a case outside the cylinder. Monte Carlo simulations were

used to test for a statistically significant difference in risks. The space–time permutation scan statistic is a variation of the space–time scan statistic in which, for the epidemic studied here, the number at risk or the size of the population at risk, would be the total number of cases identified during the epidemic, and number of cases would be the number of cases detected in each time interval, which in this study was 1 day. Here, the maximum value of the spatial window was set to include 50% of the total number of cases and the temporal window was set to include 50% of the study period, as suggested elsewhere (Kulldorf et al., 1998). A group of cases located significantly closer to each other at any time of the epidemic, compared with the expected location of cases under the null hypothesis of spatial and temporal random distribution of cases, were considered a cluster.

Results

General results

The FMD epidemic in Peru of 2004 lasted for 39 days and 26 herds were found to have animals that had clinical signs and that tested positive for FMD (Table 1). The median herd size of affected herds was 61.5 and the median number of cattle infected per herd was 3. The estimated median time-to-report an FMD case, which represented the time between owner observation of signs to reporting a suspicious case to authorities, was 3.5 days (min = 0, max = 16).

Herd reproductive ratio

The mean R_h was 5.3 on the second day of the epidemic (two outbreaks reported) and declined to 2.1 (four outbreaks reported) and 1.8 (eight outbreaks reported) by the 11th and 13th days, respectively, and to 1.3 (16 outbreaks reported) on the 25th day of the epidemic, after which time the R_h could not be estimated (Fig. 2).

Knox's test

Considering the 325 possible observed pairs of cases and using the combination of $X_t = 7$ days and $X_d = 0.5$ km, 49 pairs of cases were observed to be separated by less than the critical time and distance. The expected number of pairs of cases separated by less than the critical time and distance was 37.9 ($P = 0.047$), indicating the presence of spatio-temporal clustering. Using the combination of $X_t = 14$ days and $X_d = 0.5$ km, 90 pairs of cases were observed and 73.3 pairs of cases were expected ($P = 0.032$), indicating the presence of spatio-temporal clustering.

Results of regression analysis revealed that the difference between the number of observed and the number of expected case pairs was negatively associated ($\beta = -0.69$; CI $= -2.59, -0.55$; $P = 0.006$) with critical distance, indicating that as the distance between cases decreased, the intensity of clustering increased. The difference between the number of observed and the number of expected case pairs was not associated with critical time ($\beta = 0.143$; CI $= -0.33, 0.642$; $P = 0.498$) (Table 2).

Space–time permutation scan statistic

The space–time permutation scan statistic estimated a most likely spatio-temporal cluster that included consecutive case numbers 13, 14 and 15 of the cases, all of which were reported to authorities on the 19th day of the epidemic. The average distance between the three cases in this cluster was 0.10 km. The number of expected cases for the 19th day was 0.35, which was lower than the three cases observed on that day ($P = 0.059$).

Discussion

Despite the delay of 7 days in the identification of the index case (Table 1), the FMD epidemic in Peru in 2004

Fig. 2. Daily number of cases reported (bars) and changes in the estimated herd reproductive ratio (red line is the average; green lines are the confidence intervals) during the 2004 foot-and-mouth disease epidemic in Peru.
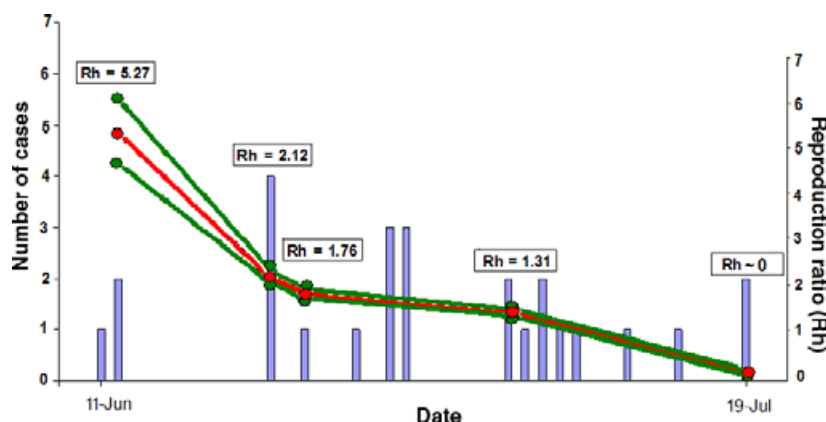
Table 2. Difference between observed and expected number of pairs of foot-and-mouth disease (FMD)-affected herds for different combinations of critical times and distances for the 2004 FMD epidemic in Peru

Critical time (days)	Critical distance (km)				
	0.5	1	2	4	8
7	11.117	4.532	1.597	−3.942	−0.660
14	16.689	9.243	1.729	−6.132	−0.357
21	10.538	10.846	4.538	−1.380	−0.154

Positive numbers indicate evidence of clustering.

was restricted to 26 herds. In contrast, the number of FMD-affected herds was higher in other epidemics in which there were similar delays in identifying and/or controlling the initial cases, such as Taiwan in 1997, where 6147 herds were affected (Yang et al., 1999), Argentina in 2000 and 2001, where 2519 herds were affected (Perez et al., 2004b) and Great Britain in 2001, where 1849 case-herds were reported between February 20 to July 15 (Gibbens et al., 2001). The small size of the epidemic could be related to a combination of lower herd density and lower number of direct and indirect contacts between herds in the region where the epidemic occurred, compared with the other FMD epidemics mentioned above. The median time from onset of infection to report a case during the Peru epidemic was 3.5 days, which was similar to a median time of 4 days calculated for the FMD epidemic in Argentina (Perez et al., 2004a). The latent period of FMD infection, which includes the eclipse phase of viral infection and the subclinical infectious period that for FMD ranges from 2 to 5 days (Burrows, 1968), can explain in part the median delay of 3.5 days estimated between the introduction of FMD into a herd and the reporting of the disease to the veterinary service.

The R_h values estimated here were substantially different than those for other recent FMD epidemics. The R_h estimated during the first week of the epidemic in Peru ($R_h = 5.3$) was twice that of the estimated R_h for the beginning of the FMD epidemics in Argentina in 2001 ($R_h = 2.4$; Perez et al., 2004a) or in the Netherlands ($R_h = 2.6$; Bouma et al., 2003). We speculate that the high value of R_h in Peru could have been related to dissemination from a single infected shipment of livestock that was split among multiple herds, and only limited contact of secondary cases, which would appear as an inflated R_h that in fact did not represent spread from herd to herd. The R_h probably decreased rapidly because of a low number of susceptible animals in a region where FMD vaccination had been systematically and aggressively conducted twice a year since 1998 (SENASA, 2004a). This interpretation is also supported by the apparent uniform temporal distribution of cases, as indicated by data collected during the epidemic (Table 1). The non-significant association ($\beta = 0.143$; CI = −0.33, 0.642; $P = 0.498$) between critical time used to estimate clustering, and the difference in the number of observed and the number of expected case pairs in the Knox test suggests that time was not as influential on the occurrence of clustering as was geographical location. This finding also supports the hypothesis of an initial common point source infection followed by a limited transmission of disease because one would expect that association between time and clustering would be significant in the event of local disease spread. Alternatively, the rapid decrease of the R_h may also be explained at least in part by the immediate restriction of animal movements in the region. A major difference between the epidemic in Peru in 2004 and the epidemics in Argentina and in the Netherlands in 2001 is that in Peru the FMDv was introduced into a population in which vaccination and other control measures already have been implemented, but in which vaccine failure or more likely vaccine management failure, may have left some animals susceptible to the infection. Therefore, the value of R_h estimated here represents the effective reproductive ratio observed in an intervened population, which differs from the value of R_h that would have been estimated in a naive population and that is commonly referred to as basic reproductive ratio. Probably because at least some of the animals in affected herds were immune to FMD infection in Peru, the proportion of infected animals in all FMD-affected herds was <4%, the cumulative incidence in 15/26 FMD-affected herds was <10% and only small herds ($n \leq 60$) had a cumulative incidence >20% (Table 1).

The methods used in this study and the values estimated using the methods described can be used to plan response operations in case of future FMD epidemics in regions with similar disease status as the district of Lurin. The values estimated for the R_h can be used as a reference number to estimate the number of possible subsequent infected herds, which in turn can be used to project the resources needed during a disease response operation, such as number of vaccine doses and staff required to control an FMD epidemic in Peru. Because the value of $R_h = 5.3$ estimated at the beginning of the epidemic might have been overestimated as a result of the potential introduction of a single shipment, the values of $R_h > 1$ subsequently estimated ($R_h = 1.3$–2.1) are probably more accurate for that purpose. PANAFTOSA (2007) recommends the establishment of a 10-km buffer zone around a case to conduct surveillance activities. The findings that the radius of the PANAFTOSA-recommended buffer zone (10 km) is higher than the maximum radius where all of the cases were located (4 km) and than the critical spatial

distance where clustering was estimated to occur (0.5 km) suggest that PANAFTOSA standard measures may be sufficient to protect against the occurrence of new FMD cases over the course of an epidemic in Peru.

In conclusion, this study provides an epidemiological analysis of data available for the 2004 FMD epidemic in Peru. The rapid decrease on the values of R_h and the limited spatial and temporal extension of the epidemic provide quantitative estimates of the self-limiting nature of the FMD spread in a region of Peru with high coverage and frequency of FMD vaccination.

Acknowledgements

References

Anderson, R. M., and R. M. May, 1991: *Infectious Diseases of Humans: Dynamics and Control*, 2nd edn. Oxford University Press, USA.

Bates, T. W., M. C. Thurmond, and T. E. Carpenter, 2003: Description of an epidemic simulation model for use in evaluating strategies to control and outbreak of foot-and-mouth disease. *Am. J. Vet. Res.* 64, 195–204.

Bergmann, I. E., V. Malirat, E. Neitzert, E. Beck, N. Panizzutti, C. Sanchez, and A. Falczuk, 2000: Improvement of a serodiagnostic strategy for foot-and-mouth disease virus surveillance in cattle under systematic vaccination: a combined system of an indirect ELISA-3ABC with an enzyme-linked immunoelectrotransfer blot assay. *Arch. Virol.* 145, 473–489.

Bouma, A., A. R. W. Elders, A. Dekker, A. de Koeijer, C. Bartels, P. Vellema, P. van der Wal, E. M. A. van Rooij, F. H. Pluimers, and M. C. M. de Jong, 2003: The foot-and-mouth disease epidemic in the Netherlands in 2001. *Prev. Vet. Med.* 57, 155–166.

Burrows, R., 1968: Excretion of foot-and-mouth disease virus prior to the development of lesions. *Vet. Rec.* 82, 387–388.

Clarke, J. B., and R. E. Spier, 1980: Variation in the susceptibility of BHK populations and cloned cell lines to three strains of foot-and-mouth disease virus. *Arch. Virol.* 63, 1–9.

Diggle, P. J., A. G. Chetwynd, R. Häggkvist, and S. Morris, 1995: Second order analysis of space–time clustering. *Stat. Methods Med. Res.* 4, 124–136.

Ferris, N. P., and M. Dawson, 1988: Routine application of enzyme-linked immunosorbent assay in comparison with complement fixation for the diagnosis of foot-and-mouth and swine vesicular disease. *Vet. Microbiol.* 16, 201–209.

Gibbens, J. C., C. E. Sharpe, J. W. Wilesmith, L. M. Mansley, E. Michalopoulou, J. B. M. Ryan, and M. Hudson, 2001: Descriptive epidemiology of the 2001 foot-and-mouth disease epidemic in Great Britain: the first five months. *Vet. Rec.* 149, 729–743.

Gobierno de Peru, 2004: Reglamento para la Prevención y Erradicación de la Fiebre Aftosa. Decreto Supremo 042–2004-AG.

Knox, G., 1964: The detection of space–time interactions. *Appl. Stat.* 13, 25–29.

Kulldorf, M., W. F. Athes, E. J. Freuer, B. A. Miller, and C. R. Key, 1998: Evaluating cluster alarms: a space–time scan statistic and brain cancer in Los Alamos, New Mexico. *Am. J. Public Health* 88, 1377–1380.

Kulldorff, M., and Information Management Services, Inc, 2003: SATSCAN v5.1: software for the spatial and space–time scan statistics. Available at: http://www.satscan.org.

Kulldorff, M., R. Heffernan, J. Hartman, R. Assunção, and F. Mostashari, 2005: A space–time permutation scan statistic for disease outbreak detection. *PLoS Med* 2, 216–224.

McVicar, J. W., and P. Sutmoller, 1970: Foot-and-mouth disease: the agar gel immunodiffusion precipitin test for antibody to virus-infection-associated (VIA) antigen as a tool for epizootiologic surveys. *Am. J. Epidemiol.* 92, 273–278.

Moonen, P., L. Jacobs, A. Crienen, and A. Dekker, 2004: Detection of carriers of foot-and-mouth disease virus among vaccinated cattle. *Vet. Microbiol.* 103, 151–160.

PANAFTOSA, 2004: Informe de resultados laboratoriales. 1–4 Laboratory report from PANAFTOSA to SENASA.

PANAFTOSA, 2007: Manual de procedimientos para la atención de ocurrencias de fiebre afotsa y otras enfermedades vesiculares.Projecto BID/PANAFTOSA – OPS/OMS para los países del MERCOSUR Ampliado.PANAFTOSA-OPS/OMS, Brazil.

Perez, A. M., M. P. Ward, and T. E. Carpenter, 2004a: Control of a foot-and-mouth disease epidemic in Argentina. *Prev. Vet. Med.* 65, 217–226.

Perez, A. M., M. P. Ward, and T. E. Carpenter, 2004b: Epidemiological investigations of the 2001 foot-and-mouth disease outbreak in Argentina. *Vet. Rec.* 154, 777–782.

Rodriguez-Torres, J. G., 2000: International approach to eradication and surveillance for foot-and-mouth disease in the Americas. *Ann. N. Y. Acad. Sci.* 916, 194–198.

Saiz, M., J. I. Nunez, M. A. Jimenez-Clavero, E. Baranowki, and F. Sobrino, 2002: Foot-and-mouth disease virus: biology and prospects for disease control. *Microbes Infect.* 4, 1183–1192.

SENASA, 2004a: *Expediente para el reconocimiento por la Organización Mundial de Sanidad Animal – OIE, de la zona sur del Perú como libre de fiebre aftosa sin vacunación*. SENASA, Lima, Peru.

SENASA, 2004b: *Informe final del programa de control establecido, para la erradicación del brote de fiebre aftosa en Lurín*. SENASA, Lima, Peru.

Sharma, S. K., P. P. Singh, and D. K. Murty, 1981: Foot and mouth disease in sheep and goats: an iceberg infection. *Indian Vet. J.* 58, 925–928.

Ward, M. P., and T. E. Carpenter, 2000: Analysis of time–space clustering in veterinary epidemiology. *Prev. Vet. Med.* 43, 225–237.

Wernery, U., and O. R. Kaaden, 2004: Foot-and-mouth disease in camelids: a review. *Vet. J.* 168, 134–142.

Yang, P. C., R. M. Chu, W. B. Chung, and H. T. Sung, 1999: Epidemiological characteristics and financial costs of the 1997 foot-and-mouth disease epidemic in Taiwan. *Vet. Rec.* 145, 731–734.

Zottele, A. C., and V. M. Astudillo, 1991: Economía de la salud animal, instrumentos de evaluación financiera y viabilidad económica. *Bol. Centr. Panam. Fiebre Aftosa.* 57, 23–41.